REMARKS

Rejections - 35 USC § 103

Claims 1-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Leonard (U.S. Patent Publication No. 2002/0028242) in view of Prater (U.S. Patent Publication No. 2004/0052846) and Karehill (U.S. Patent No. 6,605,303). Specifically, according to the Office Action, since Leonard discloses a controlled release formulation comprising paroxetine-containing core and Prater discloses a controlled release formulation with a separation layer between the core and the enteric coating, those skilled in the arts would be motivated to combine the teaching of Leonard with the formulation of Prater to arrive at the claimed invention of the present application.

However, Applicant respectfully disagrees the Office Action's reading of Prater and thus believes the claimed invention is patentable over the cited references.

The basic difference: Delayed Release technology Vs Sustained (Controlled) Release Technology

First of all, the **delayed release formulations are different from the sustained release formulation**. In the pharmaceutical field, the delayed release technology is clearly distinguishable from the sustained release technology. Particularly, the delayed release refers to a release pattern where an active ingredient contained in the formulation is not immediately disintegrated and released after administration. In other words, in the delayed release technology, the time at which the active ingredient starts to be released is deferred. An example of the delayed release formulation is an enteric coated oral medication which dissolves in the intestines and not in the stomach.

On the other hand, the sustained release refers to a mechanism to dissolve **slowly** and/or release a drug over time. Basically, the sustained release technology is totally different from the delayed release technology in that the former has nothing to do with the time at which the active ingredient starts to be released, although sometimes the sustained release technology can be used together with the delayed release technology.

Because the sustained release technology is different from the delayed release, the specific technical means used in those technologies are also different. For example, for delayed release, enteric coatings are usually used. However, for sustained release, the special matrix or reservoir formulated using polymers as well as specialized devices such as solid dispersion, nanoparticles, etc. are frequently used.

3. Prater does not disclose the sustained release technology

The Office Action states that Prater discloses a sustained release formulation with a separation layer between the core and the enteric coating that completely encloses the core. However, as is obvious from Prater, an "object of the present invention is to provide a pharmaceutical composition which is capable of **delayed and then rapid release of the active ingredient**" (paragraph [0019]) and "this invention relates to pharmaceutical preparations and especially to **delayed release** pharmaceutical preparations. More particularly, the present invention relates to **delayed release pharmaceutical formulations** which release a drug **after a delay** following administration to a patient" (paragraph [0001]). Prater discloses a delayed release formulation, not a controlled release formulation. According to Prater, it discloses a composition comprising a core which includes a drug and a disruption agent. Also, there is a regulatory membrane coating on the core formed from a mixture of a water-soluble gel forming polymer and a water-insoluble film forming polymer. However, the regulatory membrane coating in Prater serves only to defer the time at which the active ingredient starts to be released. The foregoing is obvious from paragraph [0022], "after administration of the composition to a patient there is a delay while gastric and other fluids hydrate the water soluble polymer of the regulatory membrane coating to form a gel," and paragraph [0034], "[i]n particular, changing the coating solution components and the coating level can also modify the lag time or delay time." In other words, the regulatory membrane coating disclosed by Prater is a replacement of a conventional enteric coating layer. In this connection, the Office Action stated that Prater discloses a controlled-release formulation with a separation layer between the core and the enteric coating. Applicant respectfully disagree. According to Prater's disclosure, a composition comprising a core and a regulatory membrane coating is disclosed. In Prater, no separation layer is introduced between the core and the outer coating (the regulatory membrane coating). That is,

the regulator membrane coating disclosed by Prater is merely a replacement of a conventional enteric coating, and this is different the separation layer disclosed by Applicant's claimed invention. Therefore, those skilled in the arts cannot infer the separation layer of Applicant's claimed invention from the regulatory membrane coating disclosed by Prater.

4. There is no motivation described in the cited references to arrive at Applicant's claimed invention

Where Applicant's claimed invention aims to provide a tablet having a constant release pattern rather than simply having a sustained-release or a delayed-release pattern, the prior formulation containing paroxetine has only a sustained-release or a delayed-release pattern.

Specifically, the present inventors had found that when an enteric coating layer is directly introduced on a sustained release tablet core containing paroxetine, the release behavior of the tablet significantly changes and especially they found that such release behavior of the tablet is largely subject to GET. That is, it was found that the drug release behavior of such tablet is not regulated as originally designed after the tablet is transferred into the intestines, with regard to the residence time of the tablet in the stomach. This is fully stated in the specification of the present invention and also can be seen from the examples of Table 2. [According to Table 2, the drug release rate significantly decreased because of significant changes in the originally designed drug release behavior when a sustained release tablet core comprising paroxetine was directly introduced with an enteric coating layer when tested for 2 hours in an acidic environment (of the stomach) and then transferred to a neutral condition (of the intestines)].

In this matter, the present inventors closely examined a means to regulate such change in the drug release and reached the conclusion that this problem can be prevented if a special separation layer is introduced between a tablet core comprising paroxetine and an enteric coating layer in a way that the core is completely enclosed.

Leonards, Prater and Karehill did not realize that such a specific problem occurred when the sustained-release technology is combined with the delayed release technology with respect to

paroxetine. Therefore, it is not possible for those skilled in the arts to induce the separation layer in order to solve such a specific problem.

In this regards, the Office Action stated "[h]owever, a controlled-release formulation based solely on an enteric coating of a drug containing core is dependent on the gastric emptying time," citing paragraph [0016] of Prater. However, what Prater mentioned in paragraph [0016] are conventional enteric formulations in which the solubility can vary depending on pH, and not a controlled (sustained) release formulation. The foregoing is obvious from paragraph [0016], "[t]he coated core will survive the low pH in the stomach and release its contents **rapidly** in the alkaline environment of the upper part of the intestine."

Therefore, Applicant believes that there is no motivation described in the cited references to induce the separation layer in order to solve the problem when the enteric coating is directly introduced on the core and thus Applicant's claimed invention is patentable over the cited references.

In light of the foregoing remarks, this application is considered to be in condition for allowance, and early passage of this case to issue is respectfully requested. If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 07-1850.

Respectfully submitted,

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